

Relationship between placental development and calf birth weight in beef cattle

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ABSTRACT

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Relationships between circulating concentrations of estrone sulfate and progesterone in the dam prepartum and weight of the calf and placenta at birth were evaluated at first parity in Hereford×Angus heifers ($n=27$) bred to a purebred Angus bull. Blood samples were collected from the tail vein of all heifers at 14 day intervals throughout the last trimester of gestation, and a complete placenta was obtained from 22 heifers at parturition. Estrone sulfate was measured as free estrone after incubation with sulfatase enzyme, and both estrone and progesterone levels were quantitated by radioimmunoassay. Maternal plasma estrone sulfate concentrations increased ($P<0.01$) quadratically from Day 100 to Day 10 prepartum (Day 100, 6.4 ng ml^{-1} ; Day 10, 19.0 ng ml^{-1}), and were correlated negatively ($r=-0.84$, $P<0.01$) with changes in plasma progesterone for the same period (Day 100, 11.4 ng ml^{-1} ; Day 10, 6.2 ng ml^{-1}). Birth weight was greater for male than female calves (38.3 vs. 32.9 kg , $P<0.01$), but maternal plasma estrone sulfate and progesterone concentrations and placental weights were not affected ($P>0.1$) by the sex of the fetus. Calf birth weight was correlated positively with maternal plasma estrone sulfate concentrations between Days 10 and 1 prepartum ($r=0.65$, $P<0.01$) and with the dry weight of the cotyledons ($r=0.76$, $P<0.01$), intercotyledonary membranes ($r=0.48$, $P<0.05$) and total placenta ($r=0.71$, $P<0.01$). Three neonatal calf deaths occurred; dams for two of the calves had a 50% reduction in plasma estrone sulfate concentrations for the last 20 days of gestation and a reduction in cotyledonary surface area. Collectively, these results suggest that variation among dams (i.e. either of inherent or pathological origin) for total mass and (or) function of the placentomes within the placenta may influence birth weight, and possibly neonatal viability, of calves born to first parity beef heifers. Furthermore, estrone sulfate concentrations in the maternal circulation provide an index of fetal–placental–maternal well-being and placental insufficiency in cattle.

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INTRODUCTION

Calf birth weight is highly variable and is affected by several factors including maternal, paternal and environmental effects. The reported positive correlations between calf birth weight and total placental weight or cotyledonary weight in dairy cattle (Head et al., 1981) and among fetal weight, cotyledonary weight or area and placenta weight in beef cattle (Prior and Laster, 1979) suggest that placental surface area and (or) function may influence prenatal growth of the bovine fetus. Because the bovine placentome has been identified as the major source of estrogen synthesis and of prepartum maternal concentrations of circulating estrogens (Hoffmann et al., 1979), changes in maternal concentrations of estrone sulfate may reflect changes in the interaction between the maternal-fetal units and (or) in placental function. Thus, the lower prepartum maternal estrone sulfate concentrations and smaller calf birth weights in heat-stressed dairy cows (Collier et al., 1982), and the positive correlation between prepartum maternal estrone sulfate concentrations and calf birth weight within genotypically similar (Echternkamp, 1984) and dissimilar (Guilbault et al., 1985) cattle populations may provide additional evidence that the placenta influences prenatal growth of the bovine fetus. A positive correlation between prepartum maternal concentrations of estrogens and fetal birth weight has been reported for human pregnancies (Calcagnile et al., 1980). The objective of this study was to determine the relationships among prepartum maternal concentrations of estrone sulfate, placental size and calf birth weight, and the contribution of placental insufficiency to retarded fetal growth and mortality.

MATERIALS AND METHODS

Estrus was synchronized in 30 Angus×Hereford crossbred 18-month-old heifers. All heifers were artificially inseminated with semen from one purebred Angus bull at the synchronized estrus and at the subsequent estrus; 27 heifers were palpated per rectum as pregnant at about 90 days of gestation and used in this study. Blood samples (10 ml) were collected from the tail vein into heparinized syringes at 14 day intervals from Day 180 of gestation to parturition. Blood samples were refrigerated immediately and centrifuged; plasma was collected and stored at -10°C until assayed for progesterone and estrone sulfate.

During the calving season, heifers were monitored continuously for detection of labor symptoms, administration of obstetrical assistance, and collection of the placenta at expulsion. Body weight of the calf at birth was measured within 4 h after delivery. A complete placenta was collected from 22 heifers at expulsion; placentas were weighed and frozen immediately after collection. Subsequently, placentas were thawed, cotyledons were dissected

from the chorioallantoic membranes, and the two components were weighed separately, dried at 65°C for 48 h and reweighed.

Concentrations of estrone sulfate in maternal plasma were measured by the radioimmunoassay procedure described by Eley et al. (1981). Free estrogens were extracted from duplicate 1 ml aliquots of plasma with 5 ml of diethyl ether and discarded. Subsequently, the plasma was incubated with 100 units of sulfatase enzyme at 37°C for 4 h. Liberated estrone was extracted with diethyl ether, dried under N₂, resuspended in 0.1% gel, 0.1 M phosphate-buffered saline (pH 7.0) and quantified by a single antibody, dextran-charcoal radioimmunoassay. Estrone sulfate concentrations (ng ml⁻¹) were expressed as 1.4 times the assayed estrone concentration. Production and characterization of the estrone antiserum (WII BARC No. 4) have been described previously by Guthrie and Deaver (1979). The recovery of 10, 40 or 80 pg of estrone sulfate from three volumes of plasma from a non-pregnant cow ranged from 93 to 105%. The inter- and intra-assay coefficients of variation in seven assays were 8.7% and 10%, respectively.

Progesterone was measured in duplicate 100 µl aliquots of plasma by the radioimmunoassay procedure described by Maurer and Echternkamp (1982). Two reference plasma samples included in each assay had mean concentrations of 1.2 and 9.0 ng ml⁻¹ and inter-assay coefficients of variation of 11.3 and 12.6%; intra-assay coefficients of variation were 7.5 and 10.1%.

For analysis of hormonal data, day of blood collection was referenced to parturition (Day 0), and plasma concentrations of estrone sulfate and progesterone were averaged for 10 day intervals from Day 0 to Day 100 prepartum. Changes in plasma concentrations across days of gestation were determined by split-plot analysis of variance. Relationships among birth weight of the calf, number of cotyledons per placenta, wet and dry weights of cotyledons, intercotyledonary membranes and total placenta and maternal plasma concentrations of progesterone and estrone sulfate prepartum were evaluated by regression and correlation analysis. The relationships between placental weights and calf birth weight were best described by a second-order polynomial regression equation. Effects of sex of calf on the preceding variables were analyzed by least-squares analysis of variance. Differences among means were tested using Duncan's multiple range test.

RESULTS

Concentrations of estrone sulfate in the maternal circulation increased quadratically during the last 100 days of gestation (Fig. 1). A concurrent reciprocal decrease in plasma progesterone concentrations (Fig. 1) resulted in a negative correlation between prepartum estrone sulfate and progesterone concentrations ($r = -0.84$, $P < 0.01$). Prepartum circulating concentrations of estrone sulfate and progesterone did not differ ($P > 0.05$) between heifers

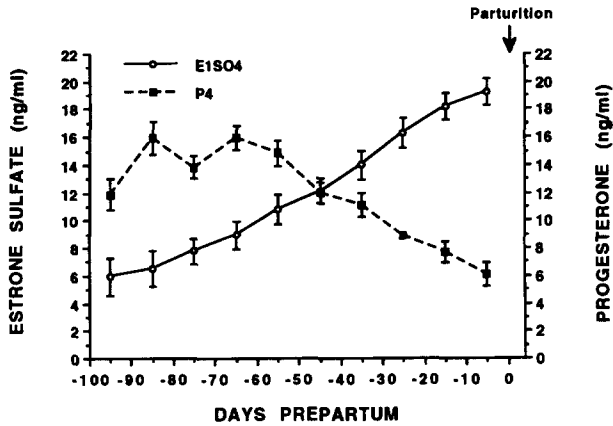


Fig. 1. Mean concentrations of estrone sulfate and progesterone in the maternal circulation for the last 100 days of gestation.

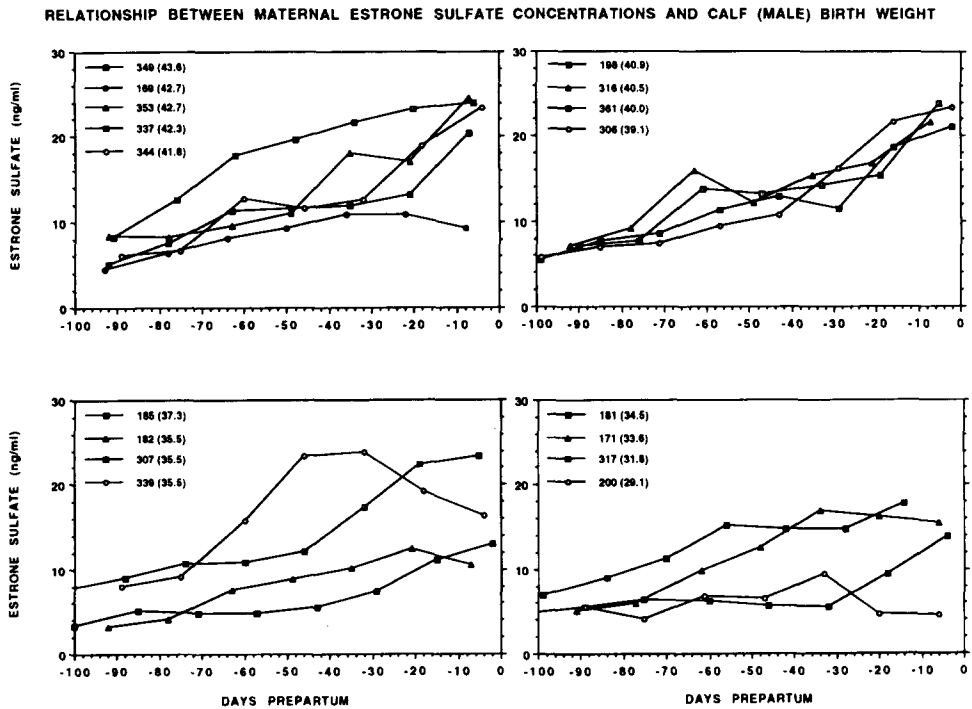


Fig. 2. The relationship between maternal estrone sulfate concentrations and calf birth weight for individual dams gestating a male calf.

gestating male and female fetuses; thus, hormonal data were combined for the two fetal groups. Maximal estrone sulfate concentrations in the maternal circulation were attained between Days 10 and 1 prepartum. Progesterone concentrations in the maternal circulation were highest between Days 60 and 100 prepartum and declined gradually from about Day 60 prepartum to parturition. The relationship between calf birth weight and maternal circulating concentrations of estrone sulfate for the last 100 days of gestation is illustrated in Fig. 2 for 17 individual dams gestating a male calf, and in Fig. 3 for eight dams gestating a female calf. Data for two dams with a male calf were omitted as they duplicated other dams. Variation in estrone sulfate concentrations among dams increased with advancing gestation. The increase in maternal estrone sulfate concentrations with gestation length was related positively with calf birth weight.

Birth weight was heavier ($P < 0.01$) for male calves (38.3 ± 0.9 kg, $n = 19$) than for female calves (32.9 ± 1.4 kg, $n = 8$). Birth weight was correlated positively with circulating concentrations of estrone sulfate for Days 1–10 prepartum in dams with male fetuses ($r = 0.84$, $P < 0.01$) or female fetuses ($r = 0.82$, $P < 0.05$), or combined ($r = 0.65$, $P < 0.01$); Days 1–10 prepartum was the period of maximal estrone concentrations in the maternal circulation. The linear relationship between calf birth weight (y) and maternal estrone sulfate concentration (x , Days 1–10 prepartum) was $y = 26.3 + 0.64x$ for male calves and $y = 17.2 + 0.79x$ for female calves. The positive correlation between calf birth weight and maternal estrone sulfate concentrations was less at earlier prepartum periods, e.g. the correlation (calf sexes combined) was $r = 0.22$ ($P > 0.05$) for Days 21–30 prepartum and $r = 0.50$ ($P < 0.05$) for Days 61–70 prepartum. Comparable correlations between calf birth weight and maternal progesterone concentrations for Days 1–10, Days 21–30 and Days 61–70 prepartum were $r = 0.11$, $r = 0.12$ and $r = 0.15$, respectively, and were not significant ($P > 0.05$).

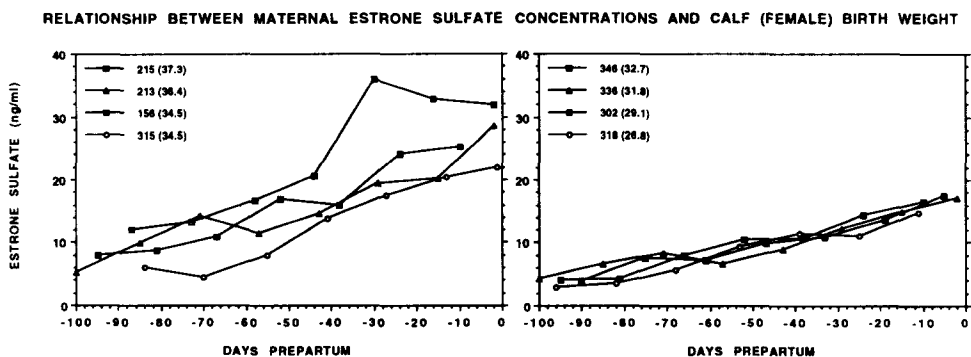


Fig. 3. The relationship between maternal estrone sulfate concentrations and calf birth weight for individual dams gestating a female calf.

TABLE 1

Comparison of birth weight of calf and placental variables between heifers gestating male or female fetuses¹

	Sex of fetus	
	Male (n = 15)	Female (n = 7)
Calf birth wt. (kg)	38.2 ± 1.1 ^a	32.8 ± 1.5 ^b
Prepartum E ₁ SO ₄ conc. (ng ml ⁻¹)	17.9 ± 1.4	19.1 ± 1.9
No. of cotyledons	75.9 ± 5.4	71.1 ± 7.4
<i>Cotyledonary wt. (g)</i>		
Wet	1308.3 ± 105.6	1528.3 ± 143.9
Dry	79.8 ± 4.6	72.8 ± 6.2
<i>Membranal wt. (g)</i>		
Wet	1653.1 ± 91.7	1820.5 ± 125.0
Dry	107.3 ± 6.5	111.0 ± 8.9
<i>Total placental wt. (g)</i>		
Wet	2961.4 ± 172.5	3348.8 ± 235.2
Dry	187.1 ± 9.4	183.8 ± 12.8

¹Only data for the 22 heifers with complete placental measurements were included in the table.

^{a,b}Calf birth weights differed significantly ($P < 0.01$).

TABLE 2

Correlations between placental weight, calf birth weight and prepartum estrone sulfate concentrations in maternal systemic circulation¹

	Calf birth weight (n = 22)	E ₁ SO ₄ concentration (n = 22)
Calf birth weight		0.65**
No. of cotyledons	0.21	0.31
<i>Cotyledonary weight</i>		
Dry	0.76**	0.72**
Wet	0.37	0.66**
<i>Membranal weight</i>		
Dry	0.48*	0.55*
Wet	0.40	0.41
<i>Total placental weight</i>		
Dry	0.71**	0.77**
Wet	0.43*	0.63**

¹Only data for the 22 heifers with complete placental measurements were analyzed by linear regression analysis.

* $P < 0.05$; ** $P < 0.01$.

Table 1 contains means (\pm SE) for birth weight of the calves and for placental measurements for the 22 heifers from which a complete placenta was obtained; 15 heifers gave birth to a male calf and seven heifers gave birth to a female calf. Wet or dry weight of the cotyledons, intercotyledonary membranes or total placenta, and number of cotyledons per placenta did not differ ($P>0.05$) between heifers with a male or female calf. Again, circulating concentrations of estrone sulfate (Days 1–10 prepartum) were similar in heifers gestating a male or female fetus.

Correlations between calf birth weight, placental measurements and maternal concentrations of estrone sulfate prepartum (Days –1 to –10) for the same 22 heifers, calf sexes combined, are presented in Table 2. Calf birth weight was correlated positively with dry weight of cotyledons ($P<0.01$),

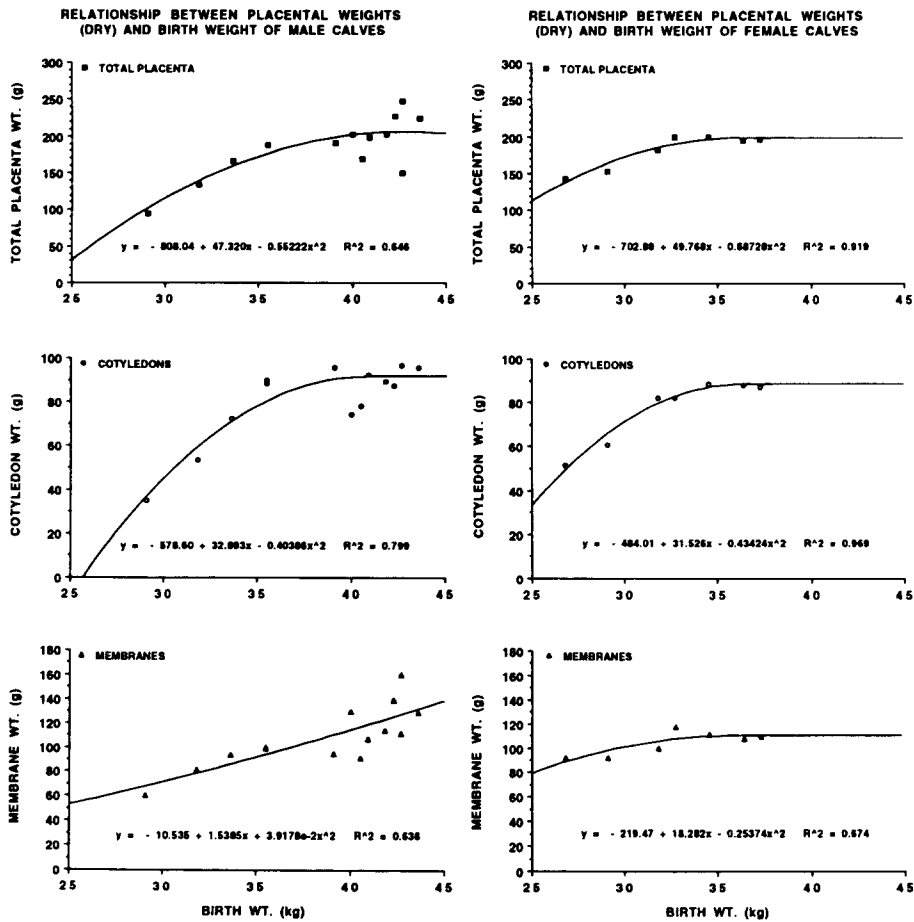


Fig. 4. Relationships between placental weights and birth weights of male ($n=15$) and female ($n=7$) calves.

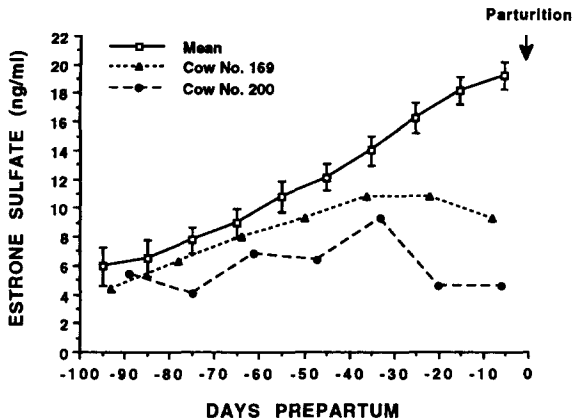


Fig. 5. Comparison of circulating concentrations of estrone sulfate for dams with (Cows 169 and 200) and without (mean) neonatal calf mortality.

intercotyledonary membranes ($P < 0.05$) and total placenta ($P < 0.01$), and with wet weight of the total placenta ($P < 0.05$). Respective correlations between birth weight and dry weight of cotyledons, intercotyledonary membranes or total placenta were $r = 0.76$, $r = 0.80$ and $r = 0.77$ for male calves ($P < 0.01$, $n = 15$), and $r = 0.76$ ($P < 0.05$), $r = 0.78$ ($P < 0.05$) and $r = 0.67$ ($P > 0.05$) for female calves ($n = 7$). Results obtained from the second-order polynomial regression analyses are presented in Fig. 4. Respective correlations between calf birth weight and dry weight of cotyledons, intercotyledonary membranes or total placenta were $r = 0.89$, $r = 0.80$ and $r = 0.80$ for male calves ($P < 0.01$) and $r = 0.98$ ($P < 0.01$), $r = 0.82$ ($P < 0.05$) and $r = 0.96$ ($P < 0.01$) for female calves. Maternal circulating concentrations of estrone sulfate (Days 1–10 prepartum) were correlated positively ($P < 0.01$) with calf birth weight, with dry weight of cotyledons, intercotyledonary membranes and total placenta, and with wet weight of the cotyledons and total placenta.

Neonatal death occurred in three of the calves. Death occurred in two calves during parturition whereas the third calf died of injuries inflicted by the dam. Fig. 5 illustrates circulating estrone sulfate concentrations for the last 100 days of gestation for the two dams whose calves died during parturition. Estrone sulfate concentrations in these two heifers differed from the mean by more than two standard deviations of the mean during the last 20–30 days of gestation. Heifer 169 gave birth to a dead, 42.5 kg, male calf. The placenta was of normal size, but gross examination revealed that about one-third of the surface area of the chorion had a leathery appearance and was essentially devoid of cotyledons; thus, cotyledonary numbers and dry weight were reduced (31 and 38.9 g, respectively). The pathological condition was diagnosed by the veterinary laboratory as mycotic placentitis. Heifer 200 gave birth to a

very small dead male calf (29 kg) with a very small placenta (total dry weight 94.9 g).

DISCUSSION

In vivo and in vitro assessments of steroid biosynthesis by bovine placentomes have indicated that the steroidogenic capacity of the placentomes for synthesis of progesterone (Hoffmann et al., 1979; Conley and Ford, 1987) and of free and conjugated estrogens (Hoffmann et al., 1979; Evans and Wagner, 1981) increases during the last trimester of pregnancy. This increased steroidogenic capacity results in an increase in estrone sulfate concentrations in the maternal circulation during this period as observed in the present and previous studies (Robertson and King, 1979; Thatcher et al., 1980; Eley et al., 1981; Collier et al., 1982; Guilbault et al., 1985). Synthesis and conjugation of estrogens within the bovine placentome occur in the fetal or cotyledonary portion of the placentome (Hoffmann et al., 1979; Evans and Wagner, 1981); the cotyledons in conjunction with the caruncles are the sites of transfer of nutrients, metabolites and steroids between the maternal and fetal units (Ferrell, 1989). Thus, the identified positive correlations among calf birth weight, wet and dry weights of cotyledons or total placenta, and prepartum concentrations of estrone sulfate in the maternal circulation are attributed to a positive relationship between metabolic and steroidogenic activity within the bovine placentomes, and between total placentome surface area and maternal-fetal interaction. The significant magnitudes of these positive relationships are interpreted as an influence of placental size and integrity on the expression of potential prenatal growth and development of the bovine fetus, as well as on prenatal or neonatal survival of the calf. It should be noted that the magnitudes of reduction in total placental weight and (or) cotyledonary weight, and in calf birth weight, were similar to the reduction produced experimentally in sheep by surgical removal of caruncles (Alexander, 1964b) or by heat stress (Alexander and Williams, 1971; Bell et al., 1989). Thus, the small calf birth weight, placental weight and estrone sulfate concentrations for some dams are considered to be evidence for the existence of placental insufficiency or impaired placental function in some cattle. Consistent with the present results, a positive relationship has been reported between calf birth weight and placental weight or cotyledonary weight in dairy cattle (Head et al., 1981), between fetal weight and placental weight, cotyledonary weight or cotyledonary area in beef cattle (Prior and Laster, 1979), and between prepartum estrone sulfate concentrations in maternal peripheral plasma and calf birth weight in Holstein heifers bred to sires of three different genotypic sizes (Guilbault et al., 1985). Likewise, heat stress of gestating dairy cattle reduces maternal circulating concentrations of estrone sulfate and, subsequently, birth weight of the calf (Collier et al., 1982), further emphasizing the biological

significance of the positive relationship between prenatal fetal growth and placental metabolic and steroidogenic activity. However, the positive correlations between the number of cotyledons per placenta and calf birth weight or prepartum maternal estrone sulfate concentrations were not significant ($P > 0.05$), suggesting that the total mass of placentomes per placenta is of greater biological significance than the total number of placentomes, even though the two are partially related. Also, the number and size of the cotyledons varied greatly among heifers. These observations on the relationships between birth weight and number or weight of cotyledons are consistent with the findings of Alexander (1964a) in sheep.

Alexander (1964b) reported that the removal of caruncles from the ovine uterus before mating reduced the total weight of the cotyledons, in spite of some compensatory cotyledary growth, and reduced lamb birth weight. Caton et al. (1984) reported that restriction of ovine fetuses to one uterine horn caused placental hypertrophy and thus placental and fetal weights were unaffected by the reduction in available endometrial surface. Compensation in mass of the fetal cotyledons was also noted in placentas from undernourished beef cows (Prior and Laster, 1979; Rasby et al., 1990); however, both fetal weight and estrogen concentrations tended to be lower in the thin cows (Rasby et al., 1990). Moderate to severe undernutrition during pregnancy resulted in reduced placental weight in sheep (Alexander and Williams, 1971; Mellor, 1983). Assessment of the physiological importance of compensatory development by the fetal cotyledons requires measurement of maternal and fetal blood flow and nutrient uptake within the placentomes.

Because the bovine placentomes are the major source of estrogen production and conjugation during gestation, measurement of prepartum estrone sulfate concentrations in maternal peripheral plasma may provide a diagnostic indicator of placental insufficiency and pathological abnormalities or diseases of the placenta, especially in cattle populations with low birth weights and (or) increased neonatal mortality. Circulating concentrations of total estriol (predominant estrogen of human pregnancy) have been measured repeatedly in pregnant women to monitor fetal well-being, and reduced concentrations were found in women with intrauterine fetal growth retardation, small-for-date syndrome (baby small for gestational age), or other placental deficiencies. However, the fetal adrenal glands and liver are the predominant sources of precursors for estrogen synthesis by the human placenta (Lanoux et al., 1985; Lavery, 1987), whereas estrogen synthesis in the bovine placentome is apparently independent of precursors supplied by the fetus (Hoffmann et al., 1979). Thus, the contributions of the bovine fetus to placental steroidogenesis and to steroid concentrations in the maternal circulation require additional clarification.

Because of the presence of both ovarian and extraovarian sources of progesterone synthesis and changes in their relative steroidogenic contributions

during gestation (Conley and Ford, 1987), the contribution of progesterone synthesis by the bovine placentome to prepartum concentrations of progesterone in the maternal circulation is less defined. Ferrell and Ford (1980) reported that the gravid uterus does not contribute significantly to circulating concentrations of progesterone in maternal blood up to 245 days of gestation. Thus, maternal concentrations of progesterone are presumably less predictive of placental or cotyledonary size and function which may account for the very low positive correlation between calf birth weight and prepartum circulating concentrations of progesterone in the dam. However, several studies have suggested a decline in luteal function (Erb et al., 1968; Wendorf et al., 1983) and progesterone production by luteal cells (Shemesh and Hansel, 1983) towards the end of gestation in the cow. Thus, the decline in progesterone concentrations in the maternal circulation, beginning at about Day 220 of gestation (Fig. 1), may reflect declining progesterone production by the corpus luteum. The low correlation between calf birth weight and progesterone concentrations contrasts with the findings of Caton et al. (1983), who reported that the rates of progesterone release both by the fetal-placental unit and by the ovary were proportional to birth weight of the lamb. However, in contrast to the cow, the placenta of the ewe becomes the predominant progesterone source early in gestation.

In summary, notable differences in placental weights and circulating concentrations of estrone sulfate existed among dams within this homogeneous population of first parity heifers. Furthermore, these differences were correlated positively with birth weight of their calves, which may suggest that variation in total size and (or) function of the placental placentomes (either of natural or pathological origin) influences development of the bovine fetus and subsequent birth weight of the calf. Although calf birth weight was correlated positively with placental weight and prepartum estrone sulfate concentrations in the maternal circulation (Days 1–10 prepartum), the increased birth weight for male calves was not associated with a difference in placental weight, cotyledonary number or weight, or circulating concentrations of estrone sulfate between dams gestating male or female fetuses. These findings suggest that differences in prenatal fetal growth between male and female fetuses result from genetic differences in fetal growth and metabolism rather than from differences in placental size and function (Bellows et al., 1990).

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